

Secreted aspartic proteases of *Candida albicans* activate the NLRP3 inflammasome.

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Abstract

In a recent report, we demonstrated that distinct members of the secreted aspartic protease (Sap) family of *Candida albicans* are able to induce secretion of proinflammatory cytokines by human monocytes, independently of their proteolytic activity and specific pH optima. In particular, *C. albicans* Sap2 and Sap6 potently induced IL-1 β , TNF- α , and IL-6 production. Here, we demonstrate that Sap2 and Sap6 proteins trigger IL-1 β and IL-18 production through inflammasome activation. This occurs via NLRP3 and caspase-1 activation, which cleaves pro-IL-1 β into secreted bioactive IL-1 β , a cytokine that was induced by Saps in monocytes, in monocyte-derived macrophages and in dendritic cells. Downregulation of NLRP3 by RNA interference strongly reduced the secretion of bioactive IL-1 β . Inflammasome activation required Sap internalization via a clathrin-dependent mechanism, intracellular induction of K(+) efflux, and ROS production. Inflammasome activation of monocytes induced by Sap2 and Sap6 differed from that induced by LPS-ATP in several aspects. Our data reveal novel immunoregulatory mechanisms of *C. albicans* and suggest that Saps contribute to the pathogenesis of candidiasis by

fostering rather than evading host immunity.

Beteiligte Forschungseinheiten

[Mikrobielle Pathogenitätsmechanismen](#) [Bernhard Hube](#) [Mehr erfahren](#)

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